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# Serendipity in perfluorinated series: unexpected synthesis of 7-(perfluoroalkyl)-2,3-dihydro-5*H*-1,4-dioxepin-5-one

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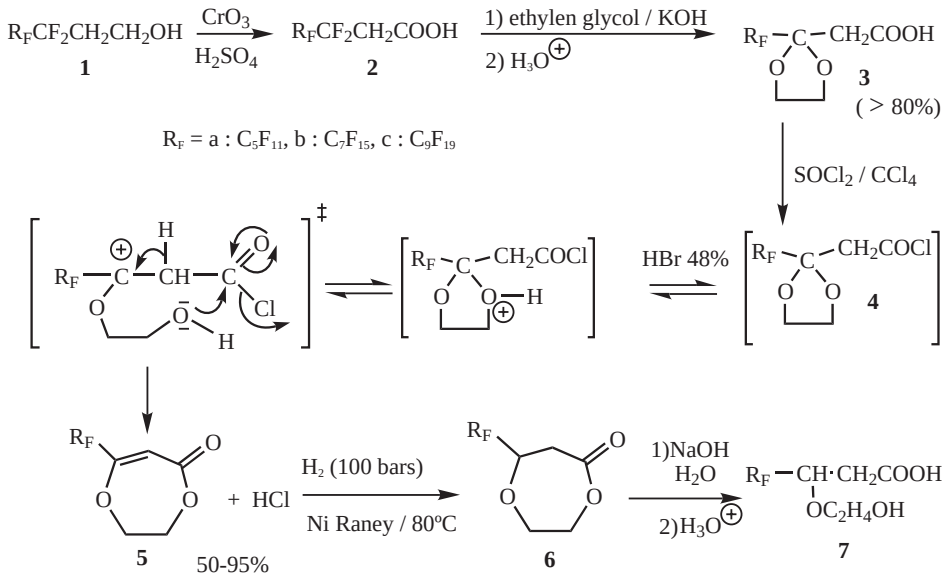
**Abstract**—Treatment of [2-(perfluoroalkyl)-1,3-dioxolan-2-yl]acetic acids with thionyl chloride and a 48% HBr solution yields 7-polyfluoroalkyl-2,3-dihydro-5*H*-1,4-dioxepine-5-one. The production of this unexpected entity is explained by a rearrangement mechanism proposed in this work. © 2001 Elsevier Science Ltd. All rights reserved.

Hydrogen substitution in a molecule by fluorine confers specific biological and physicochemical properties.[1–3] Several biological applications use fluorinated organic compounds and numerous publications are available in the literature.[4,5] The surfactants pertaining to this family are of particular interest for the preparation of fluids capable of transporting respiratory gases.[6–8] In this field, the quest for the synthesis of amphiphilic perfluorinated molecules leads us to structures containing peptidoamines.[9]

In a previous paper on the reactivity of 3-perfluoroalkylpropanoic acid **2**, we described a straightforward preparation of ketal **3**.[10] The (2-perfluoroalkyl-1,3-dioxolan-2-yl) ethanoic acid **3** was prepared from compound **2** by treatment with ethylene glycol, which was used as solvent and as reagent, and with pellets of potassium hydroxide. The overall yield from 2-perfluoro alkylethanol **1** is in the order of 70%.




**Scheme 1.** Formation and reactivity of perfluoroalkyl-oxo-lactone **5**.

*Keywords*: perfluoroalkyl; fluorinated ketal; oxolactone; rearrangement.

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With the aim of continuing our study on peptidoamines we wanted to generate α-aminoacids from α-bromo-acids derived from ketal **3**. To brominate compound **3** according to Hell/Volhard/Zelinskii, we applied the method of Harpp, describing the α-bromination of fatty acids.[11,12] Harpp proposed a two-step synthesis: first the formation in situ of acylchloride by reaction with thionyl chloride and then addition of a mixture of hydrobromic acid and *N*-bromo-succinimide. When the Harpp conditions were used on ketal **3**, the oxolactone **5** was obtained instead of the expected bromoderivative. Only thionylchloride and hydrobromic acid as catalyst are necessary to obtain lactones **5** in good yields (Scheme 1). The addition of 1 ml of HBr in a solution of acylchloride **4** prepared beforehand in carbon tetrachloride, also yields compounds **5**. These observations allowed us to propose a mechanism for this novel and unexpected rearrangement and a protocol for the preparation of compound **5**.[†]

Catalytic hydrogenation of the compounds **5** is possible but drastic conditions are needed. Raney nickel under 100 bar of hydrogen pressure and 80°C during 24 hours was needed to obtain lactones **6** with moderate yields (40–50%). Hydrolysis of **6** yields compounds **7**. Studies on the chemical and physicochemical properties of these derivatives are still under way and will be reported soon.

[†] Ketal acid **3** (2 mmol) is dissolved into 40 ml of freshly distilled thionyl chloride. The mixture is allowed to stand in reflux with stirring for 15 minutes. HBr (48%, 2 ml) is added and a reduction in temperature is observed (from 70 to 55°C). The mixture is allowed to return to room temperature after 15 minutes. The solvent is then evaporated under reduced pressure. The residue is dissolved in ethyl acetate (80 ml) and washed by water (3×100 ml). Organic phases are dried over sulphate magnesium and evaporated under reduced pressure. Yield: **5a** 97%, **5b** 83%, **5c** 75%. General characteristics of **5**: white solids (recrystallization in carbon tetrachloride), mp: **5a** 55°C, **5b** 72°C, **5c** 75°C, IR: $\nu_{[C(O)]}$: 1696 $cm^{-1}$; $\nu_{[C=C]}$: 1647 $cm^{-1}$; $^1H$ NMR (acetone/TMS/$\delta$ in ppm): $\delta = 4.87$ and 4.67, [($CH_2$-$CH_2$) 2m; $^3J_{(H\text{-}H)} = 3.2$ Hz]; $\delta = 5.74$, [(CH) s]; $^{19}F$ NMR (acetone/$CFCl_3$/$\delta$ in ppm): $\delta = -81.1$ [($CF_3$) t, $^3J_{(F\text{-}F)} = 10$ Hz]; $\delta = -116.2$ [($CF_2CO$), d, $^3J_{(F\text{-}F)} = 12$ Hz]; $\delta = -122.2$ to $-126.4$ [$(CF_2)_{n-1}$]; and $^{13}C$ NMR (acetone/TMS/$\delta$ in ppm): $\delta = 66.2$ and 74.1 [**O**$CH_2$**C**$H_2$**O**]; $\delta = 99.2$ [C=**C**-C=O]; $\delta = 110$–$120$ [$\mathbf{C}_n F_{2n+1}$]; $\delta = 150.0$ [**C**=C-C=O]; $\delta = 164.7$ [**C**=O]. Anal. for **7b** $C_{12}H_5F_{15}O_3$: calcd (found): **C**: 29.89 (29.53); **H**: 1.05 (1.07); **F**: 59.11 (59.06).

## Conclusion

A novel and unexpected rearrangement of the acetylchloride **4** of 3-perfluoroalkyl-3-dioxolane propanoic acids **3** has been highlighted. Unsaturated oxolactones **5** have been obtained. Analysis of the reaction conditions allows us to propose a mechanism for this rearrangement. These new structures could have interesting properties and the extension of this original rearrangement to similar structures is in progress.

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